

# Constraint-induced movement therapy following stroke: A systematic review of randomised controlled trials

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This systematic review investigated the effects on function, quality of life, health care costs, and patient/carer satisfaction of constraint-induced movement therapy (CIMT) for upper limb hemiparesis following stroke. A comprehensive search of the complete holdings of MEDLINE, CINAHL, EMBASE, Cochrane Library, PEDro and OTseeker to March 2005 was conducted. Fourteen eligible randomised controlled trials were identified and relevant data extracted by two independent reviewers. Effect sizes were calculated and results were pooled where possible. Method quality of the trials, assessed using the PEDro scale, had a mean score of five (range three to seven). Thirteen trials compared CIMT to an alternative treatment and/or a control group. One trial compared two CIMT protocols. Acute, subacute, and chronic conditions were studied. Effect sizes could be estimated for nine trials. Results were significant and in favour of CIMT in eight of these for at least one measure of upper limb function. The pooled standardised mean difference could be calculated for five outcome measures producing moderate to large effect sizes, only one of which attained statistical significance. Results indicate that CIMT may improve upper limb function following stroke for some patients when compared to alternative or no treatment. Rigorous evaluation of constraint-induced movement therapy using well-designed and adequately powered trials is required to evaluate the efficacy of different protocols on different stroke populations and to assess impact on quality of life, cost and patient/carer satisfaction. [Hakkennes S and Keating JL (2005): Constraint-induced movement therapy following stroke: A systematic review of randomised controlled trials. *Australian Journal of Physiotherapy* 51: 221–231]

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## Introduction

Hemiparesis is common following stroke. Reduced upper limb function impacts on ability to perform activities of daily living (Page et al 2004), which is likely to reduce independence and increase burden of care. Constraint-induced movement therapy (CIMT) is a family of techniques that have been implemented to increase the amount and quality of function of an affected upper limb. These techniques involve restraint of the intact limb over an extended period, in combination with a large number of repetitions of task-specific training of the affected limb.

CIMT evolved when it was observed that monkeys stopped using an affected upper extremity immediately after unilateral deafferentation by dorsal rhizotomy and never spontaneously resumed use (Knapp et al 1958, Knapp et al 1963, Taub 1977). It was proposed that animals could learn 'non-use' when attempts to use an affected limb immediately following injury are unsuccessful. Subsequent research identified that use of a deafferented arm could be induced by either immobilising the unaffected arm for a period of days or by training the affected arm (Taub 1980). When movement was restricted for a period of one to two days, the animal would use the limb while the restriction was in place but revert to non-use as soon as it was removed. However, when the restriction was imposed for a period of one to two weeks, use of the affected upper extremity was maintained after the restriction was removed. This mechanism of learned non-use is thought to apply in humans who suffer hemiparesis following stroke, where the initial period of motor incapacitation is due to cortical injury (Taub et al 1999).

The first investigation into the effects of CIMT on humans, involving both training of the paretic upper limb (six hours a day each weekday for two weeks) and restraint of the contralateral upper limb (90% of waking hours for 14 consecutive days) was described by Taub (1980). CIMT has continued to evolve and now constitutes a family of treatments encompassing motor restriction of the unaffected upper extremity and training of the affected extremity. For the purpose of this review, trials utilising Taub's original protocol have been defined as CIMT. Protocols in which the duration of treatment, the amount of therapy, or the constraint regimen differs from that described by Taub are referred to as 'modified' CIMT (mCIMT).

Attention was drawn to the potential harms of CIMT when lesion enlargement was described in rats given intense motor activity shortly following cortical lesion (Risødal et al 1999). Review aims therefore included examination of evidence of harms as well as of benefits.

The primary aim of this review was to assess the effectiveness of CIMT for improving upper limb function following stroke. Secondary aims were to assess effects of CIMT on quality of life and ability to perform activities of daily living. In addition, we wished to describe protocols that have been defined as CIMT and, if possible, compare the compliance/effectiveness of different protocols, describe the inclusion criteria that have been used to admit patients into trials of CIMT and document potential harms associated with CIMT such as incidence of falls or other injuries that might be a consequence of the treatment protocol. For practical application of review findings, we also considered it

important to consider intervention effects in the context of costs associated with delivering CIMT.

## Method

To identify all randomised controlled trials and systematic reviews of relevant randomised controlled trials, a computerised search of the following bibliographic databases was conducted: Medline (OVID) 1966 to Week 11, 2005; CINAHL (OVID) 1982 to Week 11, 2005; EMBASE (OVID) 1988 to Week 11, 2005; The Cochrane Library (Database of Systematic Reviews, Database of Reviews of Effects, Central Register of Controlled Trials) Issue 1, 2005; PEDro, to March 2005; and OTseeker, to March 2005.

A comprehensive search strategy was built on the search strategy of the Stroke group of the Cochrane Collaboration (Sandercock et al 2003) and utilised specific terms for identifying work in the field of CIMT. (The full search strategy is available as an eAddendum at the *Australian Journal of Physiotherapy* website.) In addition, the reference lists of all included trials were hand searched.

The two authors independently identified trials meeting the inclusion criteria, utilising title and abstract. In instances of uncertainty the full article was obtained. Disagreements between reviewers were settled through discussion. Table 1 lists the criteria for inclusion of trials.

The method quality of included trials was assessed independently by the two authors using the PEDro scale (Maher et al 2003, Moseley et al 2002). Disagreements were resolved through discussion. The PEDro scale contains ten criteria, each scoring either 1 for yes or 0 for no (Maher et al 2003). The scale assesses randomisation, allocation concealment, comparability at baseline, blinding of subjects, blinding of therapists, blinding of assessors, measurement of at least one key outcome obtained from more than 85% of the subjects initially allocated to groups, intention to treat analysis, between-group comparison tested statistically for at least one key outcome measure, and point measures and measures of variability provided for at least one key outcome measure. As blinding of subjects and therapists is impractical in trials of CIMT the maximum possible score was 8/10.

Data were extracted independently by the two authors for all included trials using a standardised form. Disagreements were resolved through discussion. Extracted data are available as an eAddendum at the *Australian Journal of Physiotherapy* website.

As all outcomes were assessed using scales considered to be continuous, the number of participants, pre- and post-intervention means, and standard deviations of measurements were extracted for all groups. In all trials where the required data were not reported, data were sought from the authors. Where possible, the effect size (Hedges *g*) for the intervention was calculated. For the purpose of this review an effect size of 0.2 to 0.49 was considered to be small, 0.5 to 0.79 moderate, and above 0.8 large (Cohen 1988).

Where appropriate, statistical pooling was performed using the method outlined by Fleiss (1993). A fixed effects model was used in cases where there was no significant between-trial variation. A random effects model was used where statistical heterogeneity was apparent. In instances where more than one comparison was available for a single outcome measure from the same trial, the more conservative estimate

**Table 1.** Criteria for inclusion of trials in this study.

- Some form of CIMT was compared with no intervention or with alternative treatment. Papers reporting CIMT provided in concert with other interventions were eligible for inclusion provided these other interventions were applied equally to comparison group(s).
- Trial participants were over 18 years and exhibited reduced functional use of an upper extremity as a result of a stroke.
- The study design was either a randomised or quasi-randomised controlled trial including cross-over designs or a systematic review of randomised controlled trials.
- The trial reported scores for at least one measure of upper limb function.
- Trials were reported in English. Funding was not available for translation.
- Results were reported in journal publications.

of effect was entered into meta-analysis.

## Results

The search yielded 1339 citations. Following exclusion based on title and abstract, 40 full articles were obtained. Four systematic reviews and 14 randomised controlled trials met inclusion criteria.

Two included reviews (van der Lee 2001, van der Lee 2003) specifically evaluated CIMT. Both were based on a previous systematic review (van der Lee et al 2001) of exercise therapy for arm function. The most recent of these reviews included only four (Dromerick et al 2000, Page et al 2002, Taub et al 1993, van der Lee et al 1999) of the 14 trials identified in this review. Neither of these reviews described study selection, data extraction methods, or validity assessment. A third included review (Barreca et al 2003) of treatment interventions for the paretic upper limb identified two trials of CIMT. Conclusions regarding effects of CIMT were constrained by the limited available evidence and no validity assessment of included trials was reported. A more recent systematic review (Van Peppen et al 2004) that assessed the impact of physical therapy on functional outcomes after stroke identified six relevant trials of CIMT. Significant results were reported in favour of CIMT for one of two pooled outcome measures.

One protocol for a systematic review of the effectiveness of traditional CIMT on stroke patients was identified (Sitori et al 2003). Results were not available.

Fourteen randomised controlled trials (Alberts et al 2004, Atteya 2004, Dromerick et al 2000, Page et al 2005, Page et al 2002, Page et al 2004, Page et al 2001, Ploughman and Corbett 2004; Ro et al in press, Sterr et al 2002, Suputtitad et al 2004, Taub et al 1993, van der Lee et al 1999, Wittenberg et al 2003) met the inclusion criteria. The trial by Ro et al (in press) was obtained from the authors to supplement the previously reported summary of results (Grotta et al 2004; Noser et al 2003).

Of the 14 trials, nine were conducted in the United States with a total of 113 participants (Alberts et al 2004, Dromerick et al 2000, Page et al 2005, Page et al 2002, Page et al 2004, Page et al 2001, Ro et al in press, Taub et al 1993, Wittenberg et al

**Table 2.** Criteria for inclusion of participants in studies.

| Criteria   | Study (first author) |          |                |          |          |           |           |                |           |          |                  |           |                |                 |
|--|----------------------|----------|----------------|----------|----------|-----------|-----------|----------------|-----------|----------|------------------|-----------|----------------|-----------------|
|  | Alberts              | Atteya   | Drom-<br>erick | Page     | Page     | Page      | Page      | Plough-<br>man | Ro        | Sterr    | Suputti-<br>tada | Taub      | van der<br>Lee | Witten-<br>berg |
|  | 2004                 | 2004     | 2000           | 2001     | 2002     | 2004      | 2005      | 2004           | in press  | 2002     | 2004             | 1993      | 1999           | 2003            |
| Time since onset of stroke                                   | 3–9 mths             | 1–6 mths | < 14 days      | 1–6 mths | 1–6 mths | > 12 mths | < 14 days | < 4 mths       | < 14 days | >12 mths | 12–120 mths      | > 12 mths | > 12 mths      | > 12 mths       |
| Age (years)  | >18                  | 18–75    | –              | 18–95    | 18–95    | 18–95     | 18–95     | < 75           | –         | –        | 18–80            | < 75      | 18–80          | –               |
| Specified diagnosis  | X                    | X        | –              | X        | X        | X         | X         | X              | –         | –        | X                | –         | X              | X               |
| Specified side of hemiplegia                                 | –                    | –        | –              | –        | –        | –         | –         | –              | –         | –        | –                | X         | X              | –               |
| Able to extend at least 10° at the fingers                   | X                    | X        | –              | X        | X        | X         | X         | –              | X         | X        | X                | X         | X              | X               |
| Able to extend at least 20° at the wrist                     | X                    | X        | –              | X        | X        | X         | X         | –              | –         | X        | X                | X         | X              | X               |
| No evidence of excessive spasticity                          | –                    | X        | –              | X        | X        | X         | X         | –              | –         | X        | –                | X         | –              | –               |
| No evidence of excessive pain                                | X                    | X        | –              | X        | X        | X         | X         | –              | –         | –        | –                | –         | –              | –               |
| Measurement of reduced upper limb function                   | X                    | –        | X              | –        | –        | –         | X         | X              | X         | –        | X                | X         | X              | X               |
| Intact sensation / protective reactions                      | –                    | –        | X              | –        | –        | –         | –         | –              | –         | –        | X                | –         | –              | –               |
| Specified level of cognitive function                        | X                    | X        | X              | X        | X        | X         | X         | X              | –         | X        | X                | X         | X              | –               |
| Specified level of communication                             | –                    | –        | –              | –        | –        | –         | –         | –              | X         | X        | X                | –         | X              | –               |
| Specified level of standing balance                          | X                    |          | –              | –        | –        | –         | –         | –              | –         | X        | X                | X         | X              | –               |
| Not participating in an active rehabilitation program        | X                    | X        | –              | X        | X        | X         | –         | –              | –         | X        | –                | –         | –              | –               |
| Not part of other experimental studies                       | –                    | X        | –              | X        | X        | X         | X         | –              | –         | –        | –                | –         | –              | –               |
| No upper limb conditions limiting use before stroke          | –                    | –        | X              | –        | –        | –         | –         | –              | –         | –        | –                | –         | –              | –               |
| No other significant medical conditions                      | X                    | –        | –              | –        | –        | –         | –         | –              | –         | –        | –                | X         | –              | –               |
| Minimum passive range of movement of the affected upper limb | X                    | –        | –              | –        | –        | –         | –         | –              | –         | –        | –                | –         | –              | –               |
| Specification of hand dominance                              | X                    | –        | –              | –        | –        | –         | –         | –              | –         | –        | –                | X         | –              | –               |

X = inclusion criteria

2003) one in the United Kingdom (15 participants) (Sterr et al 2002), one in Thailand with 69 participants (Suputtitada et al 2004), one in Saudi Arabia with six participants (Atteya 2004), one in Canada with 23 participants (Ploughman and Corbett 2004), and one in the Netherlands with 66 participants (van der Lee et al 1999).

Participants across all trials had similar diagnoses of upper limb hemiparesis following stroke. Sterr et al (2002) included two participants with traumatic brain injury in a sample of 15. Table 2 details trial inclusion criteria for participants. All trials except two (Dromerick et al 2000, Ploughman and Corbett 2004) required subjects to have a minimum of 10

degrees of active finger extension and 20 degrees of active wrist extension. A minimum level of cognitive function was specified in all except two trials (Ro et al in press, Wittenberg et al 2003). Half of the trials excluded patients if they displayed evidence of excessive spasticity (Atteya 2004, Page et al 2005, Page et al 2002, Page et al 2004, Page et al 2001, Sterr et al 2002, Taub et al 1993) and two trials (Dromerick et al 2000, Suputtitada et al 2004) required participants to have intact sensation and protective reactions.

The duration of the trial, setting, type and time of restraint, and intensity and type of therapy varied across trials (Tables 3 and 4). Four trials followed patients beyond the post-

**Table 3.** Description of restraint procedures.

| Study (first author) | Type of restraint   | Amount of restraint   | Measure of restraint compliance  |
|----------------------|---|---|--|
| Alberts 2004         | Hand placed in a mitt   | Goal of 90% of waking hours   | Nil  |
| Atteya 2004          | Hand in a mesh polystyrene-filled mitt with Velcro straps around the wrist and arm in a cotton hemi-sling                           | Every weekday for the 5 hours identified as a time of frequent arm use  | Log book   |
| Dromerick 2000       | Padded mitten   | At least 6 hours per day  | Nil  |
| Page 2001            | Hand in a mesh polystyrene-filled mitt and arm in a cotton sling  | Every weekday for the 5 hours identified as a time of frequent arm use  | Weekly telephone calls and a log book  |
| Page 2002            | Hand in a mesh polystyrene-filled mitt and arm in a cotton hemi-sling   | Every weekday for the 5 hours identified as a time of frequent arm use  | Informal in-clinic interviews and a log book                                 |
| Page 2004            | Hand in a mesh polystyrene-filled mitt with Velcro straps around the wrist and arm in a cotton hemi-sling                           | Every weekday for the 5 hours identified as a time of frequent arm use  | Log book   |
| Page 2005            | Polystyrene-filled mitt with Velcro straps around the wrist   | Every weekday for the 5 hours identified as a time of frequent arm use  | Log book   |
| Ploughman 2004       | Long, thick knitted acrylic, thumbless mitten   | Increased progressively, beginning with 1 hour per day and increased to 6 hours per day from week 2 onwards   | Weekly meeting with principal investigator to assess hours of mitten wearing |
| Ro in press          | Mitten  | Target of 90% of waking hours, except during activities where safety would be compromised by wearing the restraint  | Not described  |
| Sterr 2002           | If the patient had no balance problems – resting hand splint and arm sling<br>With balance problems – specially designed half-glove | Target of 90% of waking hours every day of the week   | Nil  |
| Suputtitada 2004     | Glove   | During therapy time   | Nil  |
| Taub 1993            | Resting hand splint and sling secured at both ends  | Worn at all times during waking hours, every day of the week, except for specific activities (e.g. toileting, where balance compromised); > 90% of waking hours | Nil  |
| van der Lee 1999     | Resting hand splint and closed arm sling, attached to the waist (sling attached during treatment only)                              | Patients instructed not to wear splint for travelling, sleeping, dressing or during toilet activities   | Log book   |
| Wittenberg 2003      | Hand splint and sling   | During waking hours   | Nil  |

intervention assessment, reporting outcomes at one month (Sterr et al 2002), three months (Ro et al in press), 12 months (van der Lee et al 1999) and 24 months (Taub et al 1993).

The method quality of included trials is detailed in Table 5. The average PEDro score of included trials was 5/10 (range 3 to 7). Although randomisation procedures appeared adequate for the trial reported by van der Lee et al (1999) 21 of 66 subjects did not stay in the group to which they were allocated. Participant eligibility criteria and treatment and control interventions were well defined in all trials.

Table 6 describes the interventions that were compared and the post-intervention between-group effect sizes for the outcome measures used in more than one trial. Meta-analyses were performed for five outcome measures and revealed moderate to large effect sizes across all calculations, only one of which attained statistical significance (Table 6). The results from the trial by van der Lee et al (1999) were excluded in the pooling due to the aberrations from the randomisation

schedule and significant differences between the groups at baseline.

#### ***Traditional CIMT versus alternative therapy or control***

Four of the thirteen trials compared traditional CIMT, or a minor variation of CIMT, to alternative therapy (Suputtitada et al 2004, Taub et al 1993, van der Lee et al 1999, Wittenberg et al 2003) and one trial compared traditional CIMT to a no treatment control (Alberts et al 2004).

All four trials comparing CIMT to alternative therapy included participants who had suffered stroke more than a year before the trial. One trial (van der Lee et al 1999) (PEDro score 6) with a sample size of 66, found significant differences between the groups on three of six outcome measures at the end of the treatment period, with moderate effect sizes (Table 6). These differences were maintained over the 12 month follow-up period. However, the authors reported that all significant between-group differences were lost when an intention-to-treat analysis was performed.



**Table 4.** Summary of trial design features.

| Study (first author) | Duration of trial             | Setting               | Intensity of therapy                           | Type of therapy   | Additional therapy  |
|----------------------|-------------------------------|-----------------------|--|---|---|
| Alberts 2004         | 2 weeks                       | Outpatient            | CIMT: 6 hours/day, 5 days/week<br>Control: Nil | One on one therapy with a rehabilitation specialist using shaping or adaptive task practice and repetitive task practice  | Nil Reported  |
| Atteya 2004          | 10 weeks                      | Outpatient            | 1/2 hour PT and 1/2 hour OT, 3 times/week      | Both: 80% of PT and OT sessions focused on neuromuscular facilitation techniques with emphasis on ADL tasks and 20% focused on compensatory techniques using unaffected side. CIMT: Identification of 2 functional tasks on the WMFT that were practised for at least 5 minutes as part of the UL program, 'shaping' techniques utilised  | Nil reported  |
| Dromerick 2000       | 2 weeks                       | Inpatient             | 2 hours/day, 5 days/week                       | CIMT: Treatment directing effort and attention to hemiparetic UL and minimising use of uninvolved UL during functional activities; circuit training encouraging use of hemiplegic arm with a variety of UL and functional tasks<br>Alternative: Standard OT treatment including compensatory techniques for ADL, UL strength and ROM and traditional positioning; circuit training program allowing bilateral self-ROM and functional activities in a supervised setting  | Routine interdisciplinary stroke treatment – individualised and circuit training techniques |
| Page 2001            | 10 weeks                      | Outpatient            | 1/2 hour PT and 1/2 hour OT, 3 times/week      | Both: 80% of PT and OT sessions focused on neuromuscular facilitation techniques with emphasis on ADL tasks and 20% focused on compensatory techniques using unaffected side. CIMT: Identification of 2 functional tasks on the WMFT that were practised for at least 5 minutes as part of the UL program, 'shaping' techniques utilised  | Nil reported  |
| Page 2002            | 10 weeks                      | Outpatient            | 1/2 hour PT and 1/2 hour OT, 3 times/week      | CIMT: OT concentrating on affected UL use in valued functional tasks, 5 min of shaping techniques to improve 2–3 valued functional tasks; PT more affected UL stretching, dynamic stand/balance activities and gait training<br>Alternative: Treated according to neuromuscular facilitation techniques for the majority of the time; some compensatory techniques also taught  | Nil reported  |
| Page 2004            | 10 weeks                      | Outpatient            | 1/2 hour PT and 1/2 hour OT, 3 times/week      | CIMT: OT 20–25 minutes concentrating on affected UL use in functional task and approximately 5 minutes of strengthening and/or compensatory techniques using the less affected UL as required; PT largely focused on lower limb activities with some time spent on UL stretching to facilitate ADLs<br>Alternative: 80% of PT and OT sessions focused on neuromuscular facilitation techniques with emphasis on functional tasks as well as stretching of the affected UL and 20% focused on compensatory techniques using unaffected side. Control: No treatment | Nil reported  |
| Page 2005            | 10 weeks                      | Outpatient            | 1/2 hour therapy session 3 times a week        | CIMT: Approximately 25 minutes, using shaping techniques, to concentrate on affected UL use in three ADL tasks chosen by the patients and the treating therapist; as required, approximately five minutes focusing on more affected UL range of movement<br>Alternative: Standard therapy for the affected UL including weight-bearing activities, manual dexterity exercises (e.g. grasp release, stacking cones) and teaching of ADLs using the less affected side  | Nil reported  |
| Ploughman 2004       | For the rehabilitation period | Inpatient/ Outpatient | As clinically indicated                        | Both groups received proximal motor control progressing to skilled task training progressing to strength and endurance training   | Not Applicable  |
| Ro in press          | 2 weeks                       | Inpatient/ Outpatient | 3 hours/day, 6 days a week                     | CIMT: Shaping technique, repeatedly presenting the performance goal to the patient, continuous  | Nil Reported  |

| Study (first author) | Duration of trial | Setting    | Intensity of therapy   | Type of therapy   | Additional therapy                                  |
|----------------------|-------------------|------------|--|---|---|
|                      |                   |            |  | verbal feedback and presenting a trial-by-trial graphic representation of performance trends<br>Alternative: Focus was to increase independence with ADLs using compensatory techniques as needed using active and/or active assisted ROM, bimanual and unilateral activities, tone modification and ADLs using modified or compensatory methods; depending on severity of motor weakness strengthening and co-ordination exercises of the affected side were also used   |   |
| Sterr 2002           | 2 weeks           | Outpatient | CIMT: 6 hours/day, every weekday<br>Alternative: 3 hrs/day every weekday | Training using a 'shaping' technique  | Nil reported  |
| Suputtitada 2004     | 2 weeks           | Outpatient | 6 hours/day every weekday  | CIMT: Affected UL training<br>Alternative: Treatment according to NDT; all activities performed bimanually and, if necessary, the affected arm was supported with the unaffected hand; symmetry of posture and inhibition of inappropriate 'synergistic' movements emphasised   | Nil reported  |
| Taub 1993            | 2 weeks           | Outpatient | CIMT: 6 hours/day, every weekday<br>Alternative: 2 PT sessions           | CIMT: Therapy consisted of a variety of tasks for the paretic UL (e.g. eating lunch with a fork and spoon, throwing a ball, playing dominoes, card games, writing on paper, writing on a chalk board, pushing a broom, Purdue Dexterity Board, Minnesota Rate of Manipulation Test)<br>Alternative: Patients told during four 10-minute periods on separate days that they had much greater motor ability with their affected upper extremity than they were exhibiting – encouraged to use the affected UL as much as possible at home; in the two PT sessions the therapist determined passive ROM, joint play, muscle tone and sensory loss; patients given self ROM exercises to carry out at home for 15 min per day, where the affected UL was passively moved into a variety of positions by unaffected UL | Nil reported  |
| van der Lee 1999     | 12 days           | Outpatient | 6 hours/day, 5 days per week   | Treatment according to NDT; all activities performed bimanually and, if necessary, the affected arm was supported with the unaffected hand; symmetry of posture and inhibition of inappropriate 'synergistic' movements emphasised; practice based on functional goals and treatment focused on housekeeping activities, handicrafts and games; groups supervised by one or two physical or occupational therapists and, if necessary, hands-on facilitation of movements and inhibition of inappropriate muscle contraction; attention paid to avoidance of associated proximal movements and to relaxation by verbal guidance   | Group activities, exercises and therapist attention |
| Wittenberg 2003      | 2 weeks           | Inpatient  | CIMT: 6 hours/day on weekdays, 4 hours/day on the weekend                | CIMT: Therapy involved progressively improving motor task performance by a successive approximation procedure during combined physical, occupational and recreational therapy<br>Alternative: 3 hrs/day, every weekday<br>Alternative: Therapy aimed to improve task performance with the unaffected UL; passive stretching to the affected UL for 1 hour during the sessions   | Nil reported  |

ADL, activity of daily living; NDT, Neuro-Developmental Therapy (Davies 1985); OT, occupational therapy; PT, physical therapy; ROM, range of movement; 'shaping' is training to achieve a specific motor objective through a series of small steps of progressively increasing difficulty so that successful performance at each step is likely to occur (Taub and Wolf 1997); UL, upper limb; WMFT, Wolf Motor Function Test

**Table 5.** Method quality of included trials.

| Study (first author) | Random allocation | Concealed allocation | Baseline comparability | Blind subjects | Blind therapists | Blind assessors | Adequate follow-up | Intention to treat analysis | Between-group comparisons | Point estimates and variability | PEDro score (/10) |
|----------------------|-------------------|----------------------|------------------------|----------------|------------------|-----------------|--------------------|-----------------------------|---------------------------|---------------------------------|-------------------|
| Alberts 2004         | Y                 | N                    | Y                      | N              | N                | N               | Y                  | Y                           | Y                         | Y                               | 6                 |
| Atteya 2004          | Y                 | N                    | Y                      | N              | N                | N               | Y                  | N                           | N                         | N                               | 3                 |
| Dromerick 2000       | Y                 | N                    | Y                      | N              | N                | Y               | Y                  | N                           | Y                         | Y                               | 6                 |
| Page 2001            | Y                 | N                    | N                      | N              | N                | Y               | Y                  | N                           | N                         | N                               | 3                 |
| Page 2002            | Y                 | N                    | N                      | N              | N                | Y               | Y                  | N                           | Y                         | N                               | 4                 |
| Page 2004            | Y                 | Y                    | Y                      | N              | N                | Y               | Y                  | N                           | Y                         | Y                               | 7                 |
| Page 2005            | Y                 | N                    | Y                      | N              | N                | Y               | Y                  | Y                           | Y                         | Y                               | 7                 |
| Ploughman 2004       | Y                 | N                    | Y                      | N              | N                | N               | N                  | N                           | Y                         | Y*                              | 4                 |
| Ro in press          | Y                 | N                    | Y                      | N              | N                | Y               | Y                  | Y                           | Y                         | Y                               | 7                 |
| Sterr 2002           | Y                 | N                    | N                      | N              | N                | N               | N                  | N                           | Y                         | Y                               | 3                 |
| Suputtitada 2004     | Y                 | N                    | Y                      | N              | N                | Y               | Y                  | N                           | Y                         | N                               | 5                 |
| Taub 1993            | Y                 | N                    | Y                      | N              | N                | Y               | Y                  | N                           | Y                         | N                               | 5                 |
| van der Lee 1999     | N                 | Y                    | N                      | N              | N                | Y               | Y                  | Y                           | Y                         | Y                               | 6                 |
| Wittenberg 2003      | Y                 | N                    | Y                      | N              | N                | Y               | Y                  | N                           | Y                         | N                               | 5                 |

\*additional data available from author on request

Insufficient data were provided to calculate the effect size using intention-to-treat data. As almost one-third of participants did not remain in the group to which they were allocated, the results of the intention-to-treat analysis command consideration.

Neither Wittenberg et al (2003) nor Taub et al (1993) matched the intensity of the therapy provided to the comparison groups. It is therefore unclear if the observed effects are attributable to therapy intensity or type. Wittenberg et al (2003) (PEDro score 6) reported large effect sizes for two of the three measures of upper limb function at the end of the intervention period, one of which achieved statistical significance (Table 6).

Taub et al (1993) (PEDro score 5), in the first randomised controlled trial investigating the effect of traditional CIMT on stroke patients, reported significant between-group differences in three measures of upper limb function. Observed differences were maintained over the two year follow-up assessment. More recently, Suputtitada et al (2004) reported significant between-group differences for two of three measures of upper limb function. Effect sizes could not be calculated from published data for either of these trials.

Alberts et al (2004) (PEDro score 6) used measures of precision grip in addition to global measures of upper limb function. They reported improvement in the treatment group for one of two measures of upper limb function but this did not attain statistical significance (Table 6). There were no significant between-group differences reported for the measures of precision grip.

**Modified CIMT versus alternative therapy or control** Eight trials (Atteya 2004, Dromerick et al 2000, Page et al 2005, Page et al 2002, Page et al 2004, Page et al 2001, Ploughman and Corbett 2004, Ro et al in press) compared mCIMT to

some form of alternative therapy. Time since onset of stroke for these trials ranged from less than 14 days (Dromerick et al 2000, Page et al 2005, Ro et al in press) to greater than 12 months (Page et al 2004).

The three trials (Dromerick et al 2000, Page et al 2005, Ro et al in press) that included patients less than 14 days post stroke were all of relatively high method quality (range 6 to 7) and all reported a large effect size in favour of the mCIMT group on their primary measure of upper limb function (Table 6). However, in the trial by Dromerick et al (2000) the constraint group was, on average, 10 years younger than the alternative treatment group, inviting the possibility that age-related condition changes may explain observed differences between groups. The duration of these trials differed between two (Dromerick et al 2000, Ro et al in press) and ten (Page et al 2005) weeks. Participants in the ten week trial received less intensive therapy over the longer duration when compared with those in the two week trial. None of these trials followed patients beyond the intervention period.

The pilot trial by Page et al (2001) (PEDro score 3) compared two subacute patients in each of three groups. The mCIMT group appeared to show improvements in upper limb function with minimal to no change in the alternative and control groups. These findings were further tested in a subsequent investigation conducted by Page et al (2002) (PEDro score 4). They reported non-significant differences between the three groups for two of three measures of upper limb function. We were unable to determine effect sizes from the published data. Atteya et al (2004) (PEDro score 3) used an identical protocol in patients one to six months post stroke. The small sample size precluded statistical analysis, however their results concurred with the earlier trial (Page et al 2001) with the mCIMT group appearing to result in improvements in upper limb function with minimal to no change in the alternative and control groups.

**Table 6.** Calculated (standardised) effect sizes and results of meta-analysis.

| Study (n)                                    | ARA<br>Effect size<br>(95% CI)*     | FIM<br>Effect size<br>(95% CI)*                           | Fugl<br>Effect size<br>(95% CI)*     | MAL<br>Effect size<br>(95% CI)* | MAL AOU<br>Effect size<br>(95% CI)* | MAL QOM<br>Effect size<br>(95% CI)* | WMFT<br>Effect size<br>(95% CI)*    |
|--|-------------------------------------|---|--------------------------------------|---------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| CIMT vs Alternative Treatment                |                                     |   |                                      |                                 |                                     |                                     |                                     |
| Suputtitada 2004 (69)                        | ID                                  |   | –                                    | –                               | –                                   | –                                   | –                                   |
| Taub 1993 (9)                                | –                                   |   | –                                    | ID                              |                                     |                                     | –                                   |
| van der Lee 1999 # (66)                      | 0.67<br>(0.16 to<br>1.19)           |   | 0.70<br>(0.18 to<br>1.21)            |                                 | 0.63<br>(0.11 to<br>1.14)           | 0.48<br>(–0.04 to<br>0.98)          | –                                   |
| Wittenberg 2003 ## (16)                      | –                                   |   | –                                    | 1.17<br>(0.10 to<br>2.24)       |                                     |                                     | <b>0.75<br/>(–0.31 to<br/>1.73)</b> |
| CIMT vs Control                              |                                     |   |                                      |                                 |                                     |                                     |                                     |
| Alberts 2004 (10)                            |                                     |   | <b>–0.82<br/>(–2.11 to<br/>0.47)</b> | –                               | –                                   | –                                   | <b>0.16<br/>(–1.08 to<br/>1.40)</b> |
| mCIMT vs Alternative Treatment               |                                     |   |                                      |                                 |                                     |                                     |                                     |
| Atteya 2004 (6)                              | UD                                  | –   | UD                                   |                                 | UD                                  | UD                                  | UD                                  |
| Dromerick 2000 (20)                          | <b>0.95<br/>(0.02 to<br/>1.87)</b>  | 0.02<br>(–0.86 to 0.90)<br>to 0.97<br>(0.04 to<br>1.90)** |                                      |                                 |                                     |                                     |                                     |
| Page 2001 (6)                                | UD                                  | –   | UD                                   |                                 | UD                                  | UD                                  | UD                                  |
| Page 2002 (14)                               | ID                                  | –   | ID                                   |                                 | ID                                  | ID                                  | –                                   |
| Page 2004 (17)                               | <b>0.92<br/>(–0.37 to<br/>2.21)</b> | –   | <b>1.42 (0.06<br/>to 2.78)</b>       |                                 | ID                                  | ID                                  | –                                   |
| Page 2005 (10)                               | <b>3.70<br/>(1.66 to<br/>5.74)</b>  | –   | <b>2.21<br/>(0.64 to<br/>3.78)</b>   |                                 | <b>6.78<br/>(3.56 to<br/>10.00)</b> | <b>4.25<br/>(2.01 to<br/>6.49)</b>  | –                                   |
| Ploughman 2004 (23)                          | <b>0.69<br/>(–0.18 to<br/>1.51)</b> | 0.57<br>(–0.27 to<br>1.41)                                |                                      |                                 |                                     |                                     |                                     |
| Ro in press (8)                              | –                                   | –   | <b>1.90<br/>(0.23 to<br/>3.57)</b>   |                                 | <b>0.36<br/>(–1.04 to<br/>1.76)</b> | <b>0.32 to<br/>(–1.08<br/>1.71)</b> | –                                   |
| mCIMT vs Control                             |                                     |   |                                      |                                 |                                     |                                     |                                     |
| Atteya 2004 (6)                              | UD                                  | –   | UD                                   |                                 | UD                                  | UD                                  | UD                                  |
| Page 2001 (6)                                | UD                                  | –   | UD                                   |                                 | UD                                  | UD                                  | UD                                  |
| Page 2002 (14)                               | ID                                  | –   | ID                                   |                                 | ID                                  | ID                                  | –                                   |
| Page 2004 (17)                               | 2.72<br>(1.21 to<br>4.24)           | –   | 2.49<br>(1.04 to<br>3.95)            |                                 | ID                                  | ID                                  | –                                   |
| CIMT vs mCIMT                                |                                     |   |                                      |                                 |                                     |                                     |                                     |
| Sterr 2002 (15)                              | –                                   | –   | –                                    |                                 | 0.57<br>(–0.47<br>to 1.60)          | 0.24<br>(–0.78 to<br>1.25)          | ID                                  |
| Pooled effect size<br>(Fixed Effects Model)  |                                     |   |                                      |                                 |                                     |                                     | <b>0.50<br/>(–0.28 to<br/>1.27)</b> |
| Pooled effect size<br>(Random Effects Model) | <b>1.51<br/>(0.27 to<br/>2.74)</b>  |   | <b>1.16<br/>(–0.18 to<br/>2.52)</b>  |                                 | <b>3.57<br/>(–2.63<br/>to 9.77)</b> | <b>2.28<br/>(–1.56 to<br/>6.12)</b> |                                     |

**Bold** text indicates data used for and results of meta-analysis; – Not Assessed; ID, insufficient data; UD, unable to determine due to small sample size; \*Based on first measurement post intervention; \*\*Represents the range of FIM scores for the 5 ADL items reported; #Based on data from final group allocation not group randomised to; ##Based on the pre-intervention standard deviation

ARA, Action Research Arm Test; FIM, Functional Independence Measure; Fugl, Fugl-Meyer Assessment; MAL, Motor Activity Log; AOU, amount of use; QOM, quality of movement; WMFT, Wolf Motor Function Test



An identical protocol of restraint, intensity of therapy, and duration of trial was used in another trial of patients greater than 12 months post stroke (Page et al 2004). For the two outcome measures for which sufficient data were available, calculated effect sizes were large and in favour of mCIMT. The effect sizes appeared larger when mCIMT was compared to a no treatment control than when compared with the alternative therapy (Table 6).

One trial (Ploughman and Corbett 2004) (PEDro score 4) found non-significant small to moderate effect sizes in favour of the constraint group on all measures of upper limb function (Table 6). In this trial, the amount and time of therapy was not standardised within or between the groups as it was administered on the basis of patient need.

**Traditional CIMT versus modified CIMT** Due to differences in trial populations it was not possible to directly compare the results of trials using a traditional CIMT protocol with those using a mCIMT protocol.

Sterr et al (2002) assessed the effects of two different CIMT protocols (PEDro score 3). Patients in this trial were more than one year post stroke; both groups received the same restraint protocol with one group receiving three and the other six hours of therapy per day. Effect sizes could be calculated for two sub-scales of the Motor Activity Log. Effects were small and moderate in favour of the six hour per day group, with neither of the between group differences achieving statistical significance (Table 5). Observed differences remained at the end of the four week follow-up period for both subscales (Amount of Use effect size 0.90; 95% CI -0.16 to 1.97 and Quality of Movement effect size 0.56; 95% CI -0.47 to 1.60).

**Activities of daily living, patient satisfaction and quality of life** Three trials (Dromerick et al 2000, Ploughman and Corbett 2004, van der Lee et al 1999) assessed activities of daily living. Two trials used the Functional Independence Measure (Dromerick et al 2000, van der Lee et al 1999), one trial used the Barthel Index (Dromerick et al 2000), and one used the Rehabilitation Activities Profile (van der Lee et al 1999). Small to large effects were found in favour of modified CIMT for five of the six measures on the Functional Independence Measure (Table 6). Only one, the upper extremity dressing item (Dromerick et al 2000), attained statistical significance. No significant differences were reported for the Barthel Index (effect size 0.57; 95% CI -0.35 to 1.44) or for the Rehabilitation Activities Profile, Personal Care (effect size -0.16; 95% CI -0.66 to 0.35) and Occupation (effect size -0.30; 95% CI -0.80 to 0.21) sub-scales.

Six trials (Atteya 2004, Page et al 2005, Page et al 2002, Page et al 2001, Taub et al 1993, van der Lee et al 1999) informally measured compliance and satisfaction with the constraint protocol through the use of interviews and/or a log book. All of these trials reported a high level of participant satisfaction and compliance. One trial (Ploughman and Corbett 2004) formally assessed compliance with the restraint. They reported poor compliance with restraint wearing, with no subjects achieving the target of six hours. The average time was 2.7 hours per day with one patient unable to wear the constraint at all.

No trials assessed quality of life.

**Harms** Two trials directly reported the harms associated with

the intervention and control treatment (Taub et al 1993, van der Lee et al 1999). The reported harms were burns (in both the reference and constraint groups), minor skin lesions (in the reference group), and muscle soreness resulting in stiffness and discomfort in the affected upper extremity (in the constraint group). In the three trials of acute patients (Dromerick et al 2000, Page et al 2005, Ro et al in press) there were no adverse events. Ploughman and Corbett (2004) reported no falls or medical complications requiring re-admission to acute care. Their measure of shoulder pain showed a non-significant increase in pain for four of the five patients in the constraint group.

**Costs** Given the intensity of therapy that is required in the CIMT protocol (up to six hours per day) the potential costs associated with CIMT could be quite high. No trials assessed the cost of implementing a CIMT protocol or compared costs to those incurred using alternative therapy.

## Discussion

A considerable research effort has assessed the effects of CIMT for upper limb hemiparesis following stroke. This review identified 14 relevant randomised controlled trials. Only one of the five outcome measures combined in meta-analysis achieved statistical significance. These results should be interpreted with some caution, given the small number of trials, the small sample sizes within the trials and the large between-trial variation in time since stroke, study quality, and the CIMT protocol. The effect sizes across the meta-analysis calculations were all moderate to large and in favour of the CIMT group. Comparable larger samples, or more trials with similar outcomes, would have indicated a statistically significant effect.

To facilitate meta-analysis, standardised measures of activity and impairment, with acceptable clinimetric properties, are desirable (Duncan et al 2000). The most common measures of upper limb function used in included trials were the Action Research Arm Test, the Wolf Motor Function Test and the Fugl-Meyer Assessment. All of these outcome measures involve the assessor scoring the participant's ability performing various tasks in a laboratory setting. They have all been shown to have a high level of reliability and validity (de Weerd and Harrison 1986, Duncan et al 1983, Fugl-Meyer et al 1975, Lyle 1981, van der Lee et al 2001, Wolf et al 2001). All trials except one used at least one of these measures to assess outcome but there was no consistency across trials in the primary outcome measure. The Motor Activity Log was developed for assessing the effectiveness of CIMT and was used in 11 of the trials included in this review. It attempts to address the problems associated with assessing upper limb function in the laboratory setting through the use of a semi-structured interview of patients and their care givers to assess the amount and quality of use of the affected upper limb in activities of daily living. This scale has been found to have good internal consistency and reliability, although its longitudinal construct validity has been questioned (van der Lee et al 2004). The implementation and scoring of the Motor Activity Log varied across trials. Lack of standardisation may account for some of the variability in effects observed using this outcome measure. It is likely that many future trials of CIMT will be conducted on small samples. To strengthen potential for meta-analysis, a standardised set of core outcome measures might be considered.

Based on the inclusion criteria for participation in included trials, only a small proportion of stroke patients may be eligible for CIMT. Two of the included trials reported information relating to patient eligibility. Of those screened, only 4% (Ro et al in press) and 18% (Taub et al 1993) were eligible for inclusion. Researchers conducting a trial currently in progress had to broaden their inclusion criteria from 3–6 months to 3–9 months post stroke due to problems with recruitment (Winstein et al 2003). Further studies aiming to determine the optimal time post stroke to implement CIMT should also consider the required inclusion criteria to maximise results and participant eligibility.

CIMT is underpinned by the theory that the duration, amount, and type of therapy combined with constraint are critical factors (Taub 1980). Page and colleagues (Page et al 2002) investigated stroke patients' and therapists' opinions of CIMT. They found that 63% of the 208 patients who returned the survey reported that they would not participate in CIMT. The main reasons provided for not wanting to participate were concerns over the length of time wearing the restrictive device and the number of days and hours in therapy. Of the 26 occupational therapists and 59 physical therapists who responded to the questionnaire, 68% thought that CIMT, when compared to other therapies, would be difficult or very difficult to administer. The primary concern of these therapists was the length of time the patients were required to spend in therapy. Therefore there is a concern that, although potentially effective, CIMT might not always be feasible. Of the eight trials that compared a modified form of CIMT with an alternative treatment, the duration of the trial was generally extended to ten weeks with participants receiving half to one hour of therapy three times per week. One trial reduced the amount of therapy from the traditional six to three hours and another trial compared six with three hours of therapy. The results for these trials indicated that a modified form of CIMT appears to be effective in improving upper limb function following stroke. The small number of trials and the limited data do not allow for conclusions regarding the optimal training frequency and duration.

With regard to the constraint, there is also cause to question patients' abilities to comply with the requirements of the protocol. In all of the trials the participants were required to wear the constraint at least five hours each day. When the constraint is worn during therapy time, ensuring adherence is possible. In the mCIMT protocols, where the majority of constraint is not under therapist supervision, compliance is more difficult to ascertain with confidence. Ploughman et al (2004) identified poor compliance with unsupervised constraint. Future studies might refine attention to compliance.

## Conclusion

This systematic review identified 14 randomised controlled trials of CIMT in stroke patients. Evidence that supports the use of CIMT is growing. CIMT may improve upper limb function following stroke compared to alternative and/or no treatment. Little can be concluded about the effects of CIMT on quality of life, independence with activities of daily living, and costs associated with the intervention. It is unclear if there is an optimal CIMT protocol. The findings of this review can be generalised to people with preserved cognitive function, 10 degrees of active finger, and 20 degrees of active wrist extension. Despite the popularity that CIMT currently enjoys amongst treatment providers, high quality trials

involving larger sample sizes are required before definitive conclusions can be drawn about the benefit of CIMT over alternative therapy or no treatment.

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